Case Report

Apical Hypertrophic Cardiomyopathy Presenting as Recurrent Unexplained Syncope

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Apical hypertrophic cardiomyopathy (AHC) is a rare variant of hypertrophic cardiomyopathy. Since its description by Sakamoto in 1976 in Japanese patients, our understanding of this entity has evolved. Although cardiac magnetic resonance imaging has emerged as the gold standard for diagnosing AHC, clinical attention must be drawn to the unique electrocardiographic features that provide the initial clues to making the diagnosis. In this case, we present a 47-year-old man with AHC who presented with recurrent syncope, but anomalies on his electrocardiogram went unnoticed on two clinical encounters. He was subsequently admitted to our service and rapidly diagnosed after we observed the very classical findings in the plain twelve lead electrocardiogram done at the time of admission. In a clinical encounter involving a patient presenting with recurrent syncope, special attention must be focused on the electrocardiogram to decipher the unique diagnostic features it might show.

Keywords: Apical hypertrophic cardiomyopathy; Syncope; Electrocardiogram; Diagnosis

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A 47-year-old man was referred from an outside facility with complaints of recurrent falls. He had been referred to a neurologist for evaluation of recurrent unexplained syncope. Each event was non-convulsive, random, and preceded by a sudden loss of balance that would progress to falling due to altered mental status. There was no apparent triggering factor, post-event confusion, or loss of either bowel or urinary continence. He had been evaluated twice at a local healthcare facility for these falls, but no cause was identified.

He was referred to us on the third presentation after suffering multiple facial and thoracic injuries. He had no evident cardiopulmonary symptoms. Because he was adopted, he had no knowledge of any family history history of cardiac events. His past medical history included bipolar disorder, tobacco abuse, alcohol dependence, and atypical facial pain. His home medications were carbamazepine, lamotrigine, olanzepine, diazepam, and venlafaxine. The only recent change in his medications was a carbamazepine dose reduction because a provider at an outside facility had thought that this might be contributing to his symptoms. On review of his past medical records (more than 10 years prior), left ventricular hypertrophy had been mentioned, but it had not been followed-up in subsequent evaluations. Previous computerized tomography (CT) of the head and neck had been unremarkable.

Clinically, the patient was alert, awake, and oriented. Blood pressure was 123/63 mmHg, pulse 83 beats/minute, temperature 99.6°F, respirations 20 breaths/minute, and oxygen saturation 95% on room air. He had no orthostatic hypotension. The physical examination was normal except for the multiple facial swellings and left-sided chest wall tenderness he had sustained from the falls.
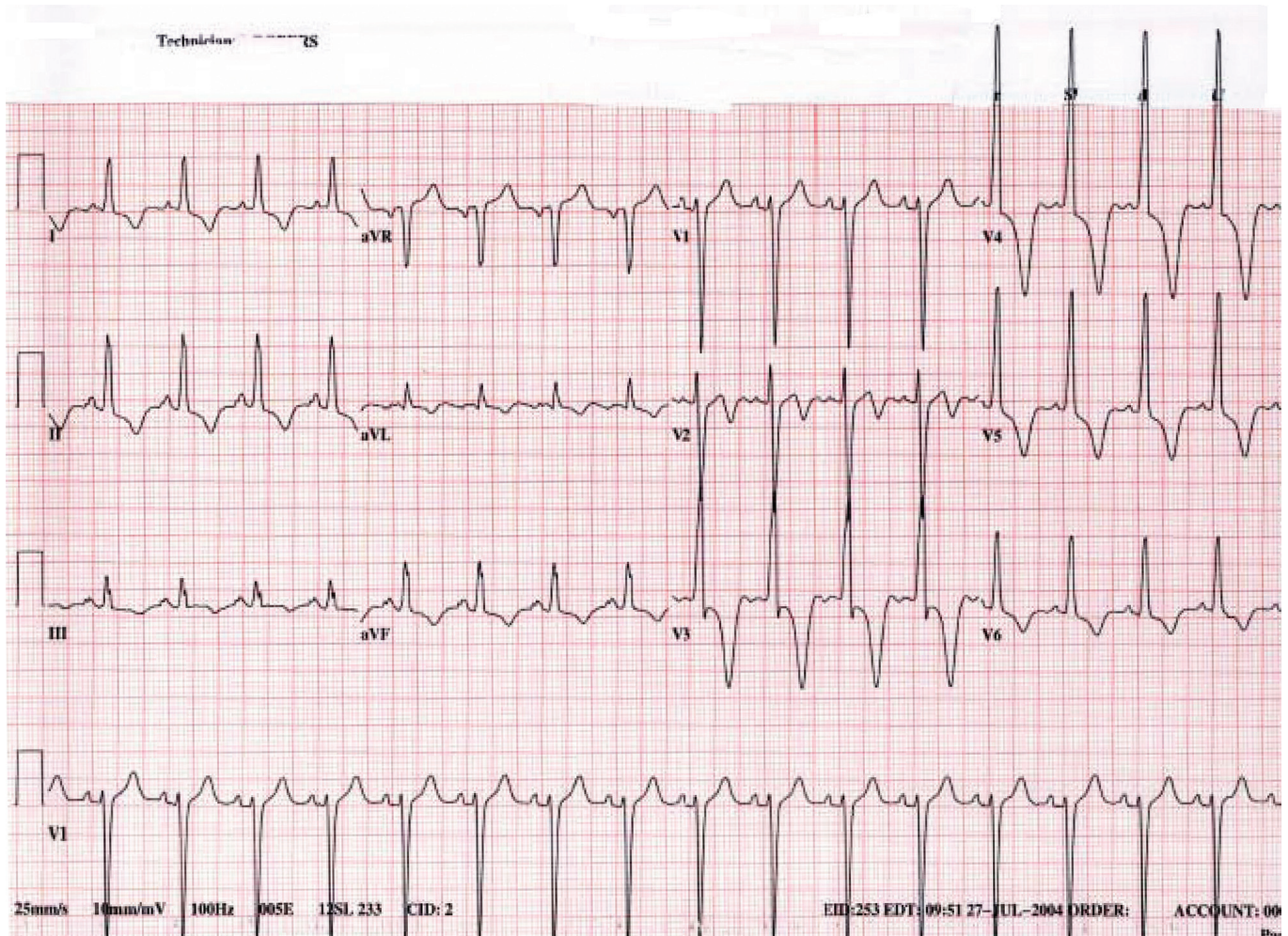
Figure 1. Resting ECG showing left ventricular hypertrophy, high QRS voltage in precordial leads (RV5+SV1=48 mm), QRS interval (80 msec), giant T-wave inversions in V3-V4 (>10 mm), and diffuse absence of septal Q-waves in I, II, III, aVF, aVL, and V3 to V6. ST-segment depression (≥ 1 mm) can also be observed in precordial leads V3 to V6. These features are descriptive of apical hypertrophic cardiomyopathy.

Resting electrocardiogram (ECG) showed left ventricular hypertrophy, high QRS voltage in precordial leads (RV5+SV1=48 mm; QRS interval 80 msec), giant T-wave inversions in V3-V4 (>10 mm), and diffuse absence of septal Q-waves in I, II, III, aVF, aVL, and V3 to V6. An ST segment depression (equal or greater than 1 mm) can also be observed in precordial leads V3 to V6 (figure 1). These features satisfy the diagnostic criteria of left ventricular hypertrophy per both Sokolow-Lyon voltage and Romhilt-Estes point score criterion and are specifically consistent with the pattern of apical hypertrophic cardiomyopathy (AHC).[1,2]

Significant laboratory results included hemoglobin 8.9 g/dL (14.2 g/dL six months earlier), with the remainder of the complete blood count, basic metabolic panel, toxicology screen, urinalysis, and cardiac enzymes within normal range. Chest radiograph and CT scan showed multiple left-sided rib fractures with a large left-sided hemothorax. A neurologist evaluated the patient and concluded that this was not seizure-like activity.

In the absence of a demonstrable neurological cause for his symptoms, and based on the quite striking findings on the ECG, a cardiogenic cause was suspected. The physical injuries were attributed to trauma. A conventional two-dimensional trans-thoracic echocardiography was initially done showing hypertrophic cardiomyopathy involving the caudal two-thirds of the left ventricle with no valvulopathy (figure 2A). However, a subsequent, more detailed contrast-enhanced echocardiography revealed apical hypertrophy with a left ventricular aneurysm (figure 2B). Based on the clinical presentation, the striking ECG manifestations (mainly in the precordial leads), and the presence of an apical aneurism, a left-sided cardiac catheterization was done, demonstrating a 90% stenosis in the posterior descending artery with no angiographic evidence of coronary artery disease in the left coronary system. The ventriculogram depicted a classic "ace of spades" appearance of the left ventricle consistent with AHC. Cardiac magnetic resonance imaging (MRI) confirmed AHC as seen with an apical aneurysm (figure 2C). Based on this evidence, the clinical conclusion was that this patient was having recurrent syncopal episodes due to AHC.
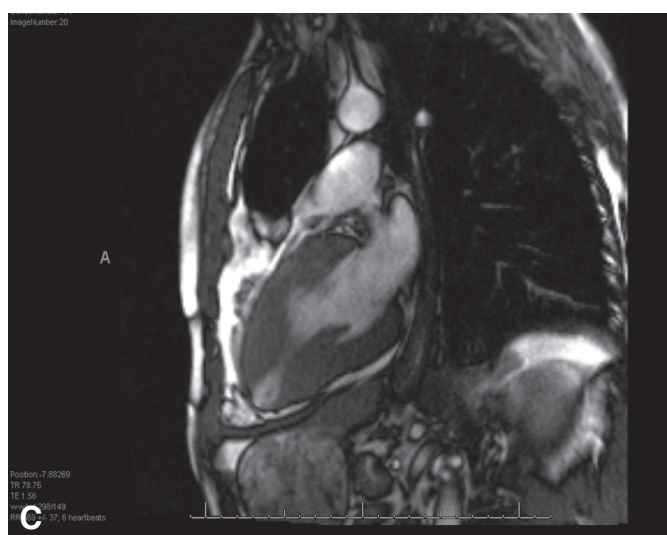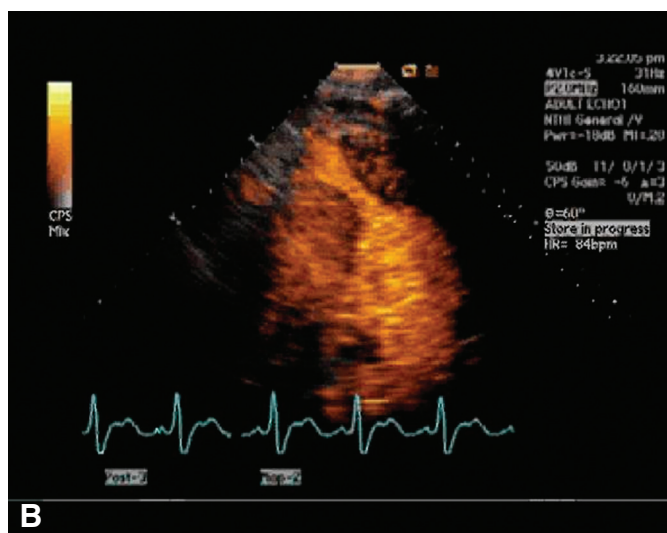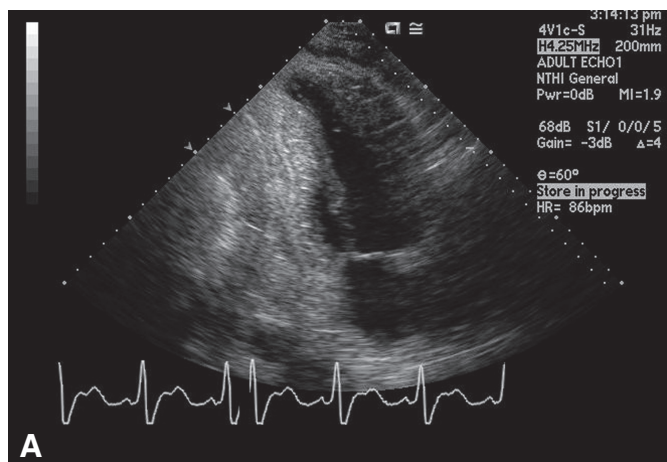
Figure 2. (A) Transthoracic echocardiography apical window images showing apical hypertrophy in diastole. (B) Contrast-enhanced transthoracic echocardiography apical window revealing hypertrophy with left ventricular apical aneurysm seen in early diastole. (C) Apical hypertrophy cardiomyopathy with an apical aneurysm as seen on cardiac MRI during diastole.

In view of the recurrent syncope and confirmed diagnosis of AHC, the patient had placement of a dual-chamber cardioverter defibrillator for prophylaxis against sudden cardiac death. Percutaneous coronary intervention to correct the significant right coronary stenosis was not considered due to absence of clinically evident angina and the presence of a large hemothorax that eventually required chest tube placement. The significant drop in hemoglobin was attributed to this hemothorax. The rest of his traumatic injuries were managed conservatively by the surgical trauma team. Follow-up one year later showed no further syncopal episodes.

Discussion

Apical hypertrophic cardiomyopathy (AHC) is a rare variant of hypertrophic cardiomyopathy first described in Asian patients.[1,3] It is more common in Asia, although it is also seen in the Western nations.[2] It is predominantly a hereditary disease, although it can also be present in patients with no family history.[4-6] In our case the patient was adopted, and no information related to his biological family was available. In the Japanese population AHC accounts for about 13% to 25% of the cases of hypertrophic cardiomyopathy,[7] but it is less prevalent in the western population.[8] Diagnostic modalities include ECG, ventriculography, nuclear myocardial perfusion studies, and MRI, which is emerging as the preferred modality.[8-10]

Apical hypertrophic cardiomyopathy can be asymptomatic or present with syncope, chest pain (symptoms similar to those of acute coronary syndromes have been described), palpitations, and dyspnea.[11] In western patients there seems to be a varied presentation as far as clinical and ECG features are concerned, compared to the classic AHC as defined in the Asian population.[11-13] Given its diverse presentation forms, plain clinical evaluation alone cannot be relied upon. In such situations, understanding the unique ECG features of AHC can be of assistance in the diagnostic process of this uncommon condition.

The presence of ECG findings indicative of left ventricular hypertrophy with giant T-wave inversions (especially in precordial leads) and loss of septal Q-wave should raise strong suspicions of AHC. These are considered pathognomnic for this disorder.[1,14] The lack of septal Q-waves is thought to be due to intra-ventricular conduction defects, whereas the giant T-wave inversions are thought to result from the reversal of repolarization order within the distal left ventricular septum and apex. The reason for the loss of Q-waves is thought to be dysfunctional activation of the ventricle, but the exact mechanism is unknown.[1] Although giant T-wave inversions in the setting of left ventricular hypertrophy are considered pathognomnic for AHC, it is relevant to have a low threshold to rule out other more frequent causes of ST-T wave abnormalities that can present with syncopal episodes as well, such as coronary heart disease, neurological diseases (eg, subarachnoid hemorrhage), medication effect (eg, digoxin), and conditions with electrolyte derrangements (eg,

hypomagnesaemia). Based on the numerous potential differential diagnoses to consider, comprehensive evaluation by cardiac imaging is necessary to confirm the diagnosis of AHC.[8-10]

Echocardiography has been universally accepted as the first-line imaging modality in investigation of patients with suspected AHC, due to its non-invasiveness, versatility, and well-established cost/benefit ratio. This continues to be true, despite its being an operator-dependent study, as well as the significant variation that might exist between the different exploratory windows.[15] Use of contrast-enhanced echocardiography can be an option in an effort to better delineate the anatomy, minimizing the above-described limitations.[16,17] A case in point is the better visualization of the left ventricular apical hypertrophy and aneurysm seen in our patient, compared to standard echocardiography, in which the apical aneurysm could not be well appreciated. Cardiac MRI is now emerging as "the gold standard" study in the diagnostic process of AHC given the limitations of echocardiography, the superiority in the assessment of the left ventricular anatomy, and its ability to detect the disease in early stages.[8,9,18,19]

Although the prevailing consensus is that AHC has a benign prognosis,[11-14] there is emerging data showing increased risk for sudden cardiac arrest, fatal arrhythmias, heart failure, and ischemic events in patients with AHC.[19-25] A recent study showed a substrate for monomorphic ventricular tachycardia to exist within the hypertrophied muscle component of AHC.[24] Management of this condition includes watchful waiting, medical treatment, or invasive interventions such as myomectomy, arrhythmia ablation, and intracardiac cardioverter defibrillator (ICD) placement.[24-26]

Although there are no randomized controlled trials specifically in AHC populations, the management of each patient relies on the risk stratification as specified in the 2002 ACC/ESC/HRS practice guidelines for management of hypertrophic cardiomyopathy.[27] Risk stratification in the general hypertrophic cardiomyopathy (HCM) population is aimed at identifying individuals who are at high risk for sudden cardiac death (SCD) and would benefit from ICD placement. Factors associated with high risk of SCD among patients with HCM are: recurrent unexplained syncope, ventricular tachyarrhythmias, massive hypertrophy (wall thickness of 30 mm or more), previous cardiac arrest, abnormal blood pressure response on treadmill stress test, high-risk mutant gene, and family history of premature HCM-related sudden death. It is recommended that all patients with HCM undergo an annual risk assessment to evaluate for presence of any of these factors.[27] Presence of each of these factors in a patient under the age of 60 years, denotes high risk for SCD and is, hence, an indication for ICD placement. This is consistent with the 2008 ACC/ESC/HRS practice guidelines for device-based therapy of cardiac rhythm abnormalities.[27-31] Our patient was 47-years-old and had recurrent, unexplained syncope which placed him at high risk for SCD; for this reason ICD placement was indicated.

In addition to the features mentioned previously, another factor that has an effect on cardiovascular outcome is the presence of apical aneurysm, which our patient had. Patients with AHC and apical aneurysm have been observed to be at higher risk of SCD, embolic stroke, and progressive cardiac failure. Although not actually recognized as an independent risk factor for indication of ICD placement, its presence should be taken into consideration when a decision about ICD placement is being made. There are limited data on whether these patients might also benefit from chronic anticoagulation in order to reduce the risk of embolic phenomena.[14,25,32]

Beta-adrenergic blocking (BB) agents were among the first drugs used for the treatment of symptomatic HCM (heart failure symptoms, chest pain, and arrhythmias). The real benefit of BB remains debatable, due to lack of large randomized trials. It could even be questionable in the AHC subgroup, especially in absence of any other indication for its use, such as systemic hypertension, cardiac arrhythmias, or coronary heart disease. Until now, use of BB and non-dihydropyridine calcium channel blockers has been, and remains, the initial drug treatment of choice for symptomatic patients, with the aim of alleviating symptoms.[29] Potential mechanisms of these benefits include their capacity to reduce heart rate at rest and exercise, negative inotropy, and the reduction on left ventricular wall stress, which consequently reduces myocardial oxygen consumption. Patients' responses remain variable, and the role of BB in asymptomatic individuals is far from established and is empiric at best. In our case, the presence of angiographically significant coronary artery disease and the concern of possible underlying ventricular tachyarrhythmia justified the use of BB. In such patients there has been demonstrable clinical benefit.[27,29]

A small group of patients with HCM are considered to be candidates for surgical intervention (myectomy). This includes patients with marked septal hypertrophy and left ventricular outflow tract obstruction, presenting with severe exertional dyspnea, NYHA class III-IV heart failure, and refractoriness to maximum medical therapy. In these types of cases the main goal is to eliminate the portion of ventricular muscle (normally the interventricular septum) that is generating the obstruction. Although some reports are available, very little is known about the utility and benefit of myectomy in patients with the AHC variant.[26,27,29] Other non-pharmacological therapies for the treatment of patients with HCM, like dual chamber pacing and ethanol septal ablation, were designed specifically (and only) to be used in the subset of patients where the site and extent of cardiac hypertrophy obstructs the left ventricular outflow. Based on the particular anatomical conditions necessary to implement these therapies, there is no room for their use in patients with the AHC variant where, by definition, no outflow tract obstruction is observed.

In 1895, Willem Einthoven reported the first accurate recording of the ECG and introduced its utility as a clinical tool. Since then the ECG has become a fundamental element in the daily diagnostic process of cardiac diseases. This is a simple study, easy to do, very available, and fairly simple to interpret, with an excellent cost/benefit ratio; in other words, is a very low cost study, and the information that it provides is invaluable. In our case, the diagnosis was almost completely established with only the classical ECG findings that had been previously overlooked. We believe that the consequence of a missed diagnosis for this patient resulted in multiple traumatic events that could have been avoided if the appropriate interpretation of the ECG had been achieved in a timely fashion. This case demonstrates a very infrequent disease in our population, and at the same time underscores the vital emphasis that must be placed on training programs, primary care physicians, and other providers involved in the evaluation and treatment of patients with syncope, in developing appropriate and adequate ECG interpretation skills.

Acknowledgments

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